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		FORM PTO-144			ATTY. DOCKET NO. 1581.0720000/RWE/TBB APPLICATION NO. U.S. Nat'l. Phase of PCT/GB99/01450				
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(W	AA1	5,405,872		04/11/1995	McDermed et al	514	605	03/22/1993	
(W	AB1	5,409,936		04/25/1995	Horma et al.	514	303	09/03/1992	
CW	AC1	5,496,569		03/05/1996	Morris, Jr. et al.	424	717	04/02/1993	
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CM	Bloch, K.D. et al., "Three Members of the Nitric Oxide Synthase II Gene Family (NOS2A, NOS2B, and NOS2C) Colocalize to Human Chromosome 17," Genomics 27:526-530, Academic Press, Inc. (1995)								
Chartrain, N.A. et al "Molecular Cloning, Structure, and Chromosomal Localization of the Human Inducible Nitric Oxide Synthase Gene," J. Biol. Chem. 269:6765-6772, The American Society for Biochemistry and Molecular Biology, Inc. (1994)									
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CW	OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Deng, A.Y. and Rapp, J.P., "Locus for the Inducible, but Not a Constitutive, Nitric Oxide Synthase Cosegregates with Blood Pressure in the Dahl Salt-sensitive Rat," J. Clin. Invest. 95:2170-2177, The American Society for Clinical Investigation, Inc. (1995)								
Cu)AS	Hare 2 Prog	Hare, J.M. and Colucci, W.S., "Role of Nitric Oxide in the Regulation of Myocardial Function," Prog. Cardiovasc. Dis. 38:155-166, W.B. Saunders Co. (1995)						
Ca	Hilbert, P. et al., "Chromosomal mapping of two genetic loci associated with blood-pressure regulation in hereditary hypertensive rats," Nature 353:521-529, Macmillian Publisher Ltd. (1991)								
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CW	Julier, C. et al., "Genetic susceptibility for human familial essential hypertension in a region of homology with blood pressure linkage on rat chromosome 10," Hum. Mol. Genet. 6:2077-2086, Oxford University Press (1997)								
	AS	3	Lacolley, P. stiffness in (1998)	acolley, P. et al., "Nitric oxide synthase gene polymorphisms, blood pressue and aortic tiffness in normotensive and hypertensive subjects," J. Hypertens. 16:31-35, Rapid Science Ltd. 1998)					
Ch	AT	3	Singh, A. et al., "Inducible Nitric Oxide Synthase in Vascular Smooth Muscle Cells From Prehypertensive Spontaneously Hypertensive Rats," Am. J. Hypertens. 9:867-877, Elsevier Science, Inc. (1996)						
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200	AS .	<u>4</u>	Takahashi, Y oxide syntha	akahashi, Y. et al., "Association analysis of TG repeat polymorphism of the neuronal nitric xide synthase gene with essential hypertension," Clin. Genet. 52:83-85, Munksgaard (1997)					
CW	AT .	4	Tambs, K. et al., "Genetic and Environmental Effects on Blood Pressure in a Norwegian Sample," Genet. Epidemiol. 9:11-26, Wiley-Liss, Inc. (1992)						
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	AS	<u>5</u>	Constitutive	Uwabo, J. et al., "Association of a Variable Number of Tandem Repeats in the Endothelial Constitutive Nitric Oxide Synthase Gene With Essential Hypertension in Japanese," Am. J. Hypertens. 11:125-128, Elsevier Science Ltd. (1998)						
0	Xu, W. et al., "Evolution of a homopurine-homopyrimidine pentanucleotide repeat sequence upstream of the human inducible nitric oxide synthase gene," Gene 204:165-170, Elsevier Science B.V. (1997)									
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